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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,707	06/30/2006	Artemis G. Hatzigeorgiou	130694.02701	1574

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EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	
MAIL DATE	**DELIVERY MODE**
12/17/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,707	HATZIGEORGIOU ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-22 and 27-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-22, 27-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 10-5-10.

Claims 12-22, 27-32 are pending in the instant application.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Applicant's arguments with respect to claims 12-22, 27-30 under 35 U.S.C. 102(e) have been considered but are moot in view of the new ground(s) of rejection set forth below.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12-22, 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over McManus et al (RNA, Vol. 8, pages 842-850 (2002)) , Chen et al (US 2005/0008617) and Vargeese et al (US 2004/0249178), the combination in view of Bentwich (USPN 7,696,342).

The claims are drawn to a computer system and computer program for identifying a micro-RNA-recognition element, which comprises a method or system for identifying and generating and preparing microRNA comprising identifying a target mRNA, generating or identifying a microRNA comprising 17-25 nucleotides which comprises a 5' proximal region between 7-9 nucleobases, which is optionally completely complementary to the target mRNA, has a single mismatch in the proximal region, or has a mismatch symmetrically placed between the 5' and 3' end of the proximal region; further comprises a loop region that is 3' to the proximal region, and which is optionally 0-9 nucleobases and which optionally comprises 2-5 non-paired sequences with the target mRNA, and/or forms a bulge of 2-3 nucleobases; and which microRNA further comprises a distal region which is 3' to the loop region, and optionally comprises either 7 contiguous complementary sequences at the 5' end of the distal region, or comprises 1-4 contiguous mismatches and has complementarity with 5 nucleobases on the distal region, including the 5' end of the distal region, which system includes an input interface and a processor for comparing mRNA sequences to

microRNA sequences, and which microRNA candidate inhibits the expression of selected target mRNA by at least 10%.

McManus et al (RNA, Vol. 8, pages 842-850 (2002)) teach the design and testing of microRNA which are directed to a preselected target mRNA sequence, and which microRNA comprise 17-25 nucleotides, and which comprises a 5' proximal region between 7-9 nucleobases, which is optionally completely complementary to the target mRNA, has a single mismatch in the proximal region, which further comprises a loop region that is 3' to the proximal region, and which is optionally between 0-9 nucleobases and optionally comprises 2-5 non-paired sequences with the target mRNA, and which further comprises a distal region which is 3' to the loop region, and optionally comprises 7 contiguous complementary sequences at the 5' end of the distal region, or comprises 1-4 contiguous mismatches and has complementarity with 5 nucleobases on the distal region, including the 5' end of the distal region (see entire document, esp. text in *Results and discussion* section, pages 843-848; Fig. 1; p. 843, Fig. 2, p. 844; fig. 3, p. 845; Fig. 4, p. 846; Fig. 6, p. 848).

Chen et al (US 2005/0008617) teach the design and assessment of iRNA molecules, including siRNA and shRNA molecules, for targeting and inhibiting mRNA expression, which iRNA molecules optionally comprise 17-25 nucleotides, and which comprise a 5' proximal region between 7-9 nucleobases, which is optionally completely complementary to the target mRNA, has a single mismatch in the proximal region, which further comprises a loop region that is 3' to the proximal region, and which is optionally between 0-9 nucleobases and optionally comprises 2-5 non-paired

sequences with the target mRNA, and which further comprises a distal region which is 3' to the loop region, and optionally comprises 7 contiguous complementary sequences at the 5' end of the distal region, or comprises 1-4 contiguous mismatches and has complementarity with 5 nucleobases on the distal region, including the 5' end of the distal region, or have a mismatch symmetrically placed between the 5' and 3' end of the proximal region, and which microRNA candidate (shRNA) inhibits the expression of selected target mRNA by at least 10% (see esp. Fig. 3, 4, 6, 7b, pages 1, 6-8, 11-13, 19-21). Chen also teaches determining free energy for the bound iRNA to a selected mRNA target sequence as a means of determining the binding affinity between the iRNA and its target sequence (see esp. paragraph 0086).

Vargeese et al (US 2004/0249178) teach the structures and inhibitory activities of various short interfering nucleic acids, including siRNA, dsRNA, and micro-RNA, and their design and use for inhibiting the expression of a target gene of known sequence (see esp. paragraphs 0416, 0577, 0578).

The primary references do not teach computer systems or programs for identifying microRNA-recognition elements.

Bentwich (USPN 7,696,342) teaches computer systems, including bioinformatic gene detection engines, for collecting data obtained from detecting and analyzing micro RNA (miRNA) genes, as well as their respective target binding sites, and comparing miRNA molecules with their target gene binding sites, and monitoring the miRNA's ability to inhibit target gene expression (see esp. figures 1-3 and the text describing those figures).

It would have been obvious to generate microRNA comprising the steps instantly claimed because McManus mad generated microRNA utilizing most of the steps claimed, in producing microRNA which provides efficient and effective target gene inhibition, which microRNA comprise essentially all of the characteristics as instantly claimed, and McManus provides a comparison of microRNA activity as a function of the positions and frequency of mismatches, loops and bulges. Moreover, Chen teaches the design and testing of microRNA molecules, as well as siRNA molecules, which molecules are tested as a function of inserted mismatches in the various sections of the dsRNA molecules as instantly claimed, as well as loops and bulges. The prior art therefore discloses the routine experimentation involved in designing the microRNA molecules as instantly claimed, and testing them for their ability to inhibit target gene expression. One therefore would have had a reasonable expectation of success that microRNA molecules with the characteristics claimed would provide for effective target gene inhibition. It was routine in the art to design and test microRNA molecules of the lengths as instantly claimed, before and after inserting bulges, mismatches and loops in the various segments of the molecule, and compare them to other siNAs for target gene inhibition, relying on the combined teachings of McManus, Chen and Vargeese.

One would have been motivated to use computer systems and programs for analyzing the data accumulated in testing the design of microRNA, comparing optimal design choices with the target sequences of the target genes, because this computer capability was well known in the art, and used routinely in determining the relationship between target gene sequences and microRNA molecules, as taught previously by

Bentwich. The computer software was readily accessible, and used to routinely to acquire larger amounts of bioinformatic data than single assays would provide.

For these reasons, the instant invention would have been obvious to one of skill in the art at the time of filing.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** The examiner's office hours are generally Monday-Friday, 10:30am - 7pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita, can be reached on (571) 272-2876. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
12-15-10

/Jane Zara/

Primary Examiner, Art Unit 1635